CLAIMS

1. A method of monitoring exposure of a person to an environmental pollutant, comprising the step of:

determining at two or more time points the presence of one or more mutations in mitochondrial DNA (mtDNA) in a body fluid of a person exposed to an environmental pollutant;

comparing the amount of mutations in mtDNA at different time points, wherein the amount of mutations correlates with amount of exposure to the environmental pollutant.

2. A method of monitoring exposure of a person to an environmental pollutant, comprising the step of:

measuring prevalence of one or more mutations in mitochondrial DNA (mtDNA) in a body fluid of a person exposed to an environmental pollutant, wherein a measured prevalence of one or more mutations in mtDNA of greater than 1% indicates clonal expansion of cells which harbor the one or more mutations in the person.

3. A method of monitoring exposure of a person to an environmental pollutant, comprising the step of:

measuring one or more mutations in a D-loop of mitochondrial DNA (mtDNA) in a body fluid of a person exposed to an environmental pollutant, wherein the number of mutations in mtDNA correlates with exposure to the environmental pollutant.

4. The method of claim 1, 2, or 3 wherein the body fluid is urine.

5. The method of claim 1, 2, or 3 wherein the body fluid is saliva.

6. The method of claim 1, 2, or 3 wherein the body fluid is sputum.

7. The method of claim 1, 2, or 3 wherein the body fluid is bronchoalveolar lavage.

8. The method of claim 1, 2, or 3 wherein mutations in mtDNA are measured with reference to mtDNA isolated from a normal tissue of the human.

9. The method of claim 8 wherein the normal tissue is paraffin-embedded.

10. The method of claim 1, 2, or 3 wherein mutations in mtDNA are measured with reference to mtDNA isolated from a blood, serum, or plasma sample of the human.

11. The method or claim 1 or 2 wherein mutations in mtDNA are measured by analysis of a gene encoding NADH dehydrogenase 4.

12. The method of claim 1 or 2 wherein mutations in mtDNA are measured by analysis of a gene encoding 16S rRNA.

13. The method of claim 2 wherein prevalence of one or more mutations in mtDNA in the body fluid is measured over time, whereby clonal expansion of cells can be monitored.

14. The method of claim 1 or 2 wherein mutations in mtDNA are measured by analysis of a cytochrome b gene.

15. The method of claim 1, 2, or 3 wherein the mutated mtDNA is found to bear a silent mutation.

16. The method of claim 1 or 2 wherein the mutated mtDNA is measured by analysis of non-coding regions.

17. The method of claim 1, 2, or 3 wherein the mutated mtDNA is measured by amplifying mtDNA segments of about 10 bp to about 4 kb.

18. The method of claim 1, 2, or 3 wherein the mutated mtDNA is measured by amplifying mtDNA segments of about 10 bp to about 2 kb.

19. The method of claim 1, 2, or 3 wherein the mutated mtDNA is measured by amplifying mtDNA segments of about 2 kb to about 4 kb.

20. The method of claim 1, 2, or 3 wherein the mutated mtDNA is measured by an oligonucleotide mismatch ligation assay.

21. The method of claim 1, 2, or 3 wherein the environmental pollutant is cigarette smoke.

22. The method of claim 1, 2, or 3 wherein the environmental pollutant is a biological toxin.

23. The method of claim 1, 2, or 3 wherein the environmental pollutant is radiation.

24. The method of claim 1, 2, or 3 wherein the environmental pollutant is industrial waste.

25. The method of claim 1, 2, or 3 wherein the environmental pollutant is chemical.

26. The method of claim 1, 2, or 3 wherein the environmental pollutant is water-borne.

27. The method of claim 1, 2, or 3 wherein the environmental pollutant is air-borne.

28. The method of claim 1, 2, or 3 wherein the environmental pollutant is a drug.

29. A kit for monitoring exposure of a person to environmental pollutants, comprising:

one or more primers which hybridize to a mitochondrial D-loop for making a primer extension product; and

written material identifying mutations which are found in the D-loop as a result of exposure to one or more environmental pollutants.

30. The kit of claim 29 further comprising a buffer.

31. The kit of claim 29 further comprising nucleic acid probes for hybridization to the extension product.

32. The kit of claim 29 wherein the primers are for PCR.

33. The kit of claim 29 wherein the primers are for a ligation assay.

34. The method of claim 3 wherein the mutation is selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide

16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; and A→G at nucleotide 16300.

35. The kit of claim 29 wherein the written material identifies a mutation selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; and A→G at nucleotide 16300.

36. The method of claim 11 wherein the mutation is selected from the group consisting of: A→G at nucleotide 10792, C→T at nucleotide 10793, C→T at nucleotide 10822, A→G at nucleotide 10978, A→G at nucleotide 11065, G→A at nucleotide 11518, C→T at nucleotide 12049, T→C at nucleotide 10966, and G→A at nucleotide 11150.

37. The method of claim 12 wherein the mutation is selected from the group consisting of: G→A at nucleotide 2056, T→C at nucleotide 2445, T → C at nucleotide 2664, and G→A at nucleotide 3054.

38. The method of claim 14 wherein the mutation is Δ 7 amino acids at nucleotide 15642.

39. An oligonucleotide probe comprising a sequence of at least 10 contiguous nucleotides of a human mitochondrial genome, wherein the oligonucleotide comprises a mutation selected from the group consisting of: a mutation selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide

195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T → C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ 7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; G→A at nucleotide 3054; T→C substitution at position 710; T→C substitution at position 1738; T→C substitution at position 3308; G→A substitution at position 8009; G→A substitution at position 14985; T→C substitution at position 15572; G→A substitution at position 9949; T→C substitution at position 10563; G→A substitution at position 6264; A insertion at position 12418; T→C substitution at position 1967; and T→A substitution at position 2299.

40. An oligonucleotide primer comprising a sequence of at least 10 contiguous nucleotides of a human mitochondrial genome, wherein the oligonucleotide comprises a mutation selected from the group consisting of: a mutation selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T

at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T → C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ 7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; G→A at nucleotide 3054;T→C substitution at position 710; T→C substitution at position 1738; T→C substitution at position 3308; G→A substitution at position 8009; G→A substitution at position 14985; T→C substitution at position 15572; G→A substitution at position 9949; T→C substitution at position 10563; G→A substitution at position 6264; A insertion at position 12418; T→C substitution at position 1967; and T→A substitution at position 2299.

41. A method to aid in detecting the presence of tumor cells in a patient, comprising:

determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient, wherein the tumor is not a colorectal tumor; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

42. A method to aid in detecting the presence of tumor cells in a patient, comprising:

determining the presence of a mutation in a D-loop of a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

43. The method of claim 42 wherein the mutation is selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; and A→G at nucleotide 16300.

44. A method to aid in detecting the presence of tumor cells in a patient, comprising:

determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a cancer of the patient but not in normal tissue of the patient, wherein the cancer is selected from the group of cancers consisting of: lung, head and neck, bladder, brain, breast, lymphoma, leukaemia, skin, prostate, stomach, pancreas, liver, ovarian, uterine, testicular, and bone; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

45. A method to aid in detecting the presence of tumor cells in a patient, comprising:

step for determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient, wherein the cancer is selected from the group of cancers consisting of: lung, head and neck, and bladder; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

46. A method to aid in detecting the presence of tumor cells in a patient, comprising:

determining the presence of a mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide 302; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ΔC at nucleotide 302; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T → C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ 7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; and G→A at nucleotide 3054; and

identifying the patient as having a tumor if one or more mutations are determined in the mitochondrial genome of the cell sample of the patient.

47. The method of claim 41, 42, 44, 45, or 46 wherein the cell sample is from blood.

48. The method of claim 41, 42, 44, 45, or 46 wherein the cell sample is from urine.

49. The method of claim 41, 42, 44, 45, or 46 wherein the cell sample is from sputum.

50. The method of claim 41, 42, 44, 45, or 46 wherein the cell sample is from saliva.

51. The method of claim 41, 42, 44, 45, or 46 wherein the cell sample is from feces.

52. The method of claim 41, 42, 44, 45, or 46 wherein the step for determining comprises amplifying mitochondrial DNA.

53. The method of claim 41, 42, 44, 45, or 46 wherein the step for determining comprises sequencing mitochondrial DNA.

54. The method of claim 41, 42, 44, 45, or 46 wherein the step for determining comprises hybridization of DNA amplified from the mitochondrial genome of the cell sample to an array of oligonucleotides which comprises matched and mismatched sequences to human mitochondrial genomic DNA.

55. The method of claim 41, 42, 44, 45, or 46 wherein the mutation is a substitution mutation.

56. The method of claim 41, 42, 44, 45, or 46 wherein the mutation is a one basepair insertion.

57. The method of claim 41, 42, 44, 45, or 46 wherein the mutation is a one basepair deletion.

58. The method of claim 41, 42, 44, 45, or 46 wherein the mutation is a transition mutation.

59. The method of claim 41, 42, 44, 45, or 46 wherein the mutation is a homoplasmic mutation.

60. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 710.

61. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 1738.

62. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 3308.

63. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A substitution at position 8009.

64. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A substitution at position 14985.

65. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 15572.

66. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A substitution at position 9949.

67. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 10563.

68. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A substitution at position 6264.

69. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an A insertion at position 12418.

70. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C substitution at position 1967.

71. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→A substitution at position 2299.

72. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 10071.

73. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 10321.

74. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 12519.

75. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 5521.

76. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 12345.

77. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 114.

78. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a ΔC at nucleotide 302.

79. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→A at nucleotide 386.

80. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an insert T at nucleotide 16189.

81. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a A→C at nucleotide 16265.

82. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a A→T at nucleotide 16532.

83. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 150.

84. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 195.

85. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a ΔC at nucleotide 302.

86. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→A at nucleotide 16183.

87. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 16187.

88. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 16519.

89. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 16380.

90. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 75

91. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an insert C at nucleotide 302.

92. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an insert CG at nucleotide 514.

93. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 16172.

94. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 16292.

95. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an A→G at nucleotide 16300.

96. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is an A→G at nucleotide 10792.

97. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 10793.

98. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 10822.

99. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a A→G at nucleotide 10978.

100. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a A→G at nucleotide 11065.

101. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 11518.

102. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a C→T at nucleotide 12049.

103. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 10966.

104. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 11150.

105. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 2056.

106. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 2445.

107. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T → C at nucleotide 2664.

108. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 10071.

109. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 10321.

110. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a T→C at nucleotide 12519.

111. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a Δ 7 amino acids at nucleotide 15642.

112. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 5521.

113. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 12345.

114. The oligonucleotide probe of claim 39 or primer of claim 40 wherein the mutation is a G→A at nucleotide 3054.

115. The method of claim 2 wherein the mutation was identified previously in a tumor of the patient.

116. The method of claim 115 wherein the patient has received anti-cancer therapy and the step for determining is performed at least three times to monitor progress of the anti-cancer therapy.

117. The method of claim 1 further comprising a step for testing a normal tissue of the patient to determine the absence of the mutation.